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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,379	11/17/2003	Tony Hunter	066671-0085	4384

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,379	HUNTER ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4 and 7-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 7-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (claim 4) in the reply filed on 8/15/2005 is acknowledged. The traversal is on the ground(s) that all of Groups (I-IV) have common thread. Thus, a search for Pin1 will uncover prior art pertinent of any combination or all of the Groups.

These have been considered, but not found persuasive. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The groups I-IV are distinct inventions, which are drawn to the methods using different materials and having different method steps. The inventions require different biological samples for determining the modulator of Pin1 and treating the patients. Although search any of the method would include the search of Pin1, the method of determining whether a composition modulating Pin 1 and the method for treating a cell proliferate disorder in a subject comprising administering Pin1 inhibitor or enhancer require different materials and have different method steps and different effects. Search required for each group is not required for the other groups because each group requires a different non-patent literature search due to each group comprising different material and/or method steps. For this reason, the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made **FINAL**.

Applicant's request to correct the record of restriction of group II (claim 5 in part) is acknowledged. The restriction of invention group II is corrected as the following:

> Claim 5 in part, drawn to a method for treating a cell proliferate disorder in a subject, comprising administering an amount of **Pin1 inhibitor** to induce mitotic arrest and nuclear fragment, classified in class 424, subclass 184.1.

Claim 4 has been amended. Claims 1-3 and 5-6 have been cancelled. Claims 7-19 have been added. Claims 4 and 7-19 are pending and examined on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

As drawn to written description:

Claims 4, 7-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims encompass a method of determining whether a composition modulates the activity of Pin1 or a functional fragment thereof. The specification states that Pin1 is a polypeptide including function fragments of the polypeptide, as long as the activity of Pin1 remains (page 8, line 27-30). The specification also states that Pin1 polypeptide includes the amino acid sequence SEQ ID NO: 2 and conservative variation thereof, which denotes the replacement of an amino acid residue by another, biologically similar residue. Therefore, the claims are inclusive of a genus of fragments, variants, a polypeptide of SEQ ID NO: 2. However, the written description in this case only sets forth Pin1 polypeptide (SEQ ID NO: 2) containing a WW domain and a PPIase domain in figure 2 A.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13,

2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of polypeptides that encompass the genus of Pin 1 protein or functional fragments, in which their activities are modulated by a composition, nor does it provides a description of structural features that are common to the Pin1 protein associated with protein-protein interaction and PPIase activity. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of *the species of* polypeptides insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) and functional attribute(s) of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only the activity of Pin1 protein (SEQ ID NO: 2), which is modulated by a composition, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the

written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

As drawn to enablement:

Claims 4, 7-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

The set of claims are broadly drawn to a method for determining whether a composition modulate Pin1 activity comprising Pin1 protein (SEQ ID NO: 2) and a functional fragment thereof. The claims are further drawn to Pin1 activity comprising protein-protein interaction and peptidyl-prolyl isomerase (PPIase) activity. The claims are further drawn to the functional fragments of Pin1 comprising at least amino acid residues 5-43 and 59-163 of SEQ ID NO: 2.

To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provide an enabling disclosure of how to make and use a claimed invention. The method objective of claims is a method for determining whether a composition modulates Pin1 activity. Thus, it would be expected that one of skill in the art would be able to determine a composition to modulate the Pin1 activity without undue experimentation by using the claimed method.

The specification, on page 4, paragraph 5, states that the invention provides a method for identifying a composition that modulates Pin 1 activity. The specification also states that controlling the

cell growth by inhibiting mitosis promoting function of NIMA, which interacts with Pin1 protein (page 18, para 3). The specification further states that controlling the growth of a cell comprises contacting the cell with a composition, which modulates Pin1 activity, for example, an inhibitor of Pin, such as a PPIase inhibitor, an anti-Pin1 antibody, or antisense inhibitor for Pin1 (page 4, para 4). However, the specification does not teach any working example, which enables the composition in the claims that modulates the activity of Pin1 protein and its functional fragments. The specification does not teach any working example having identified a composition or to identity a composition, which could modulate the activity of Pin1 and its functional fragments. The specification does not teach any identified inhibitor or enhancer for Pin1 in the art, which could decrease or increase the cell growth. The specification does not provide any teaching on a composition, which could modulate the interaction of Pin1 protein or its functional fragments with NIMA or could inhibit the PPIase activity of Pin1 protein.

The specification, on page 35 paragraph 1, further teach that the PPIase activity of Pin 1 was not inhibited by either cyclosporine A or FK520 (the inhibitors for other families of PPIases), therefore, Pin1 is a member of the third family of PPIases. However, the specification does not provide any teaching on the molecular structure of any inhibitor for the third family of the PPIases. The specification does not provide any working example to test the inhibitory function of any known or unknown molecule to the PPIase activity of Pin1 and its functional fragments. Thus, the instant specification fails to disclose the necessary parameters for using the method, which would lead to the determination of a composition that modulate the Pin1 activity.

It is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). It is also know in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor

binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein. Therefore, an undue experimentation is required to test any of claimed composition having a modulating function for any protein, which is even a minor different in its structure or sequence from a known protein.

Since the specification does not provide claimed method for determining or identifying a composition, since the specification does not provide any guidance for identifying a modulator for Pin 1 or its functional fragment, one skilled in the art would not know how to use the claimed method to determine the composition modulating the activity of Pin1 and its functional fragment on the basis of teachings in the prior art or instant specification.

In view of the lack of guidance, lack of examples, and lack of predictability associated with regard to determine whether a composition modulates Pin1 activity, one skilled in the art would be forced into under experimentation in order to practice the broadly claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-4.30pm Monday to Friday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao, Ph.D.
Examiner
Art Unit 1642

LY

SHEELA HUFF
PRIMARY EXAMINER